Amendments to the Claims

I. Amendments

Please cancel claims 1-4, 15, 21, 22 and 56-95, without prejudice or disclaimer, as directed to non-elected inventions.

II. The Claims of the Application

Claims 1-4. **(Withdrawn)**

Claim 5. **(Currently Amended)** A method for assaying **a metabolically active whole cell** for the presence or activity of an enzyme ~~**in a metabolically active whole cell**~~, comprising the steps:

(a) incubating said metabolically active whole cell with a substrate of said enzyme or an analyte compound in the presence of an agent that enhances uptake of said substrate or analyte, said agent being present at a concentration sufficient to enhance the uptake of said substrate or analyte compound;

(b) assaying **said metabolically active whole cell** for any change in concentration of said substrate or analyte compound or of a product formed via action of said enzyme on said substrate or analyte; wherein a change in said concentration is indicative of the presence or activity of said enzyme in said metabolically active whole cell**; and wherein said agent that enhances uptake of said substrate or analyte is selected from the group consisting of glycerol, dimethyl sulfoxide (DMSO), trehalose, glutamate, betaine, ethylene glycol, threitol, ribose, and trimethylamine N-oxide, with the proviso that when said agent is dimethyl sulfoxide (DMSO), said agent will be present at a concentration of between about 20% and about 60% (v/v)**.

Claim 6. (**Original**) The method of claim 5, wherein said enzyme is selected from the group consisting of a 5' nucleotidase, acetylcholinesterase, an acid phosphatase, an acidic esterase, an acidic esterase I, an acidic esterase II, an acidic non-specific esterase, an adenosine deaminase, an adenosine monophosphate deaminase, an alkaline phosphatase, an aminopeptidase A, an aminopeptidase B, an aminopeptidase M, an Aminopeptidase N, an angiotensin converting enzyme, a caspase, a cathepsin B, a cathepsin B1, a cathepsin C, a cathepsin D, a cathepsin H, a cathepsin L, a cholinesterase, a cholinesterase, a chymotrypsin, a collagenase, a cytosine deaminase, a DPP I, a DPP II, a DPP IV, an elastase, an endopeptidase I, an endopeptidase II, an ester proteinase, a galactopyranosidase, a glucoronidase, a glutathione, a glycopyranossidase, a guanine deaminase, an HIV Protease, a lipase, a membrane associated endopeptidase I, a membrane associated endopeptidase II, a neutral endopeptidase, a neutral esterase, a neutral esterase I, a neutral esterase II, a neutral non-specific esterase, a nucleosidase, a pancreatin, a phospholipase A, a phospholipase C, a phospholipase D, a plasmin, a serine phosphatase, a tartrate resistant phosphatase, a tartrate resistant phosphatase, a threonine phosphatase, a thymidine deaminase, a tripeptidyl peptidase, a trypsin, a tyrosine phosphatase, a urokinase, a v-thrompsin, and a γ-GT.

Claim 7. (**Original**) The method of claim 6, wherein said enzyme is a caspase.

Claim 8. (**Original**) The method of claim 7, wherein said caspase is caspase 1, caspase 3, caspase 6, caspase 8 or caspase 9.

Claim 9. (**Original**) The method of claim 5, wherein said substrate or analyte compound of said enzyme and said agent that enhances uptake are mixed during said incubation.

Claim 10. (**Original**) The method of claim 5, wherein said substrate or analyte compound of said enzyme and said agent that enhances uptake are not mixed during said incubation.

Claim 11. (**Original**) The method of claim 5, wherein multiple enzymes are assayed simultaneously assayed.

Claim 12. (**Original**) The method of claim 5, wherein multiple enzymes are sequentially assayed.

Claim 13. (**Currently Amended**) The method of claim 5, wherein said substrate or analyte compound comprises ~~**comprising**~~ an indicator group and one or more leaving groups, each of said leaving groups being selected for cleavage by said enzyme, said indicator group being in a first state when bonded to a leaving group, and being in a second state when said leaving group is cleaved from said indicator group by said enzyme; and wherein said step (b) comprises sensing whether said second state of said indicator group is produced; wherein the production of said second state of said indicator group is indicative of the presence or activity of said enzyme in said metabolically active whole cell.

Claim 14. (**Original**) The method of claim 13, wherein said indicator group is a fluorescent, colorimetric, bioluminescent or chemiluminescent indicator group.

Claim 15. (**Cancelled**) The method of claim 5 or claim 13, wherein said uptake-enhancing agent is selected from the group consisting of glycerol, dimethyl sulfoxide (DMSO), trehalose, glutamate, betaine, ethylene glycol, threitol, ribose, and trimethylamine N-oxide**, with the proviso that when said agent is dimethyl sulfoxide (DMSO), said agent**

will be present at a concentration of between about 20% and about 60% (v/v).

Claim 16. (**Currently Amended**) The method of **claim 5**, wherein said uptake-enhancing agent is glycerol.

Claim 17. (**Original**) The method of claim 16, wherein said glycerol concentration is between about 5% and about 60% (v/v).

Claim 18. (**Original**) The method of claim 17, wherein said glycerol concentration is between about 20% and about 60% (v/v).

Claim 19. (**Original**) The method of claim 18, wherein said glycerol concentration is between about 25% and about 40% (v/v).

Claim 20. (**Currently Amended**) The method of **claim 5**, wherein said uptake-enhancing agent is dimethyl sulfoxide (DMSO).

Claim 21. (**Cancelled**) The method of claim 20, wherein said dimethyl sulfoxide concentration is between about 5% and about 60% (v/v).

Claim 22. (**Cancelled**) The method of claim 21, wherein said dimethyl sulfoxide concentration is between about 20% and about 60% (v/v).

Claim 23. (**Currently Amended**) The method of **claim 5**, wherein said uptake-enhancing agent is glutamate.

Claim 24. (**Original**) The method of claim 23, wherein said glutamate concentration is between about 0.25 M and about 2.0 M.

Claim 25. (**Original**) The method of claim 24, wherein said glutamate concentration is between about 1 M and about 2 M.

Claim 26. (**Currently Amended**) The method of **claim 5**, wherein said uptake-enhancing agent is betaine.

Claim 27. (**Original**) The method of claim 26, wherein said betaine concentration is about 0.3 M or greater.

Claim 28. (**Currently Amended**) The method of **claim 5**, wherein said uptake-enhancing agent is trehalose.

Claim 29. (**Original**) The method of claim 28, wherein said trehalose concentration is between about 0.1 M and about 1.5 M.

Claim 30. (**Currently Amended**) The method of **claim 5**, wherein said uptake-enhancing agent is ethylene glycol.

Claim 31. (**Original**) The method of claim 30, wherein said ethylene glycol concentration is between about 2 M and about 7 M.

Claim 32. (**Currently Amended**) The method of **claim 5**, wherein said uptake-enhancing agent is threitol.

Claim 33. (**Original**) The method of claim 32, wherein said threitol concentration is between about 1 M and about 5 M.

Claim 34. (**Currently Amended**) The method of **claim 5**, wherein said uptake-enhancing agent is ribose.

Claim 35. (**Original**) The method of claim 34, wherein said ribose concentration is between about 0.4 M and about 4 M.

Claim 36. (**Currently Amended**) The method of **claim 5**, wherein said uptake-enhancing agent is triethylamine N-oxide.

Claim 37. (**Original**) The method of claim 36, wherein said triethylamine N-oxide concentration is between about 0.4 M and about 4 M.

Claim 38. (**Original**) The method of claim 13, wherein said enzyme is selected from the group consisting of a 5' nucleotidase, acetylcholinesterase, an acid phosphatase, an acidic esterase, an acidic esterase I, an acidic esterase II, an acidic non-specific esterase, an adenosine deaminase, an adenosine monophosphate deaminase, an alkaline phosphatase, an aminopeptidase A, an aminopeptidase B, an aminopeptidase M, an Aminopeptidase N, an angiotensin converting enzyme, a caspase, a cathepsin B, a cathepsin B1, a cathepsin C, a cathepsin D, a cathepsin H, a cathepsin L, a cholinesterase, a cholinesterase, a chymotrypsin, a collagenase, a cytosine deaminase, a DPP I, a DPP II, a DPP IV, an elastase, an endopeptidase I, an endopeptidase II, an ester proteinase, a galactopyranosidase, a glucoronidase, a glutathione, a glycopyranossidase, a guanine deaminase, an HIV Protease, a lipase, a membrane associated endopeptidase I, a membrane associated endopeptidase II, a neutral endopeptidase, a neutral esterase, a neutral esterase I, a neutral esterase II, a neutral non-specific esterase, a nucleosidase, a pancreatin, a phospholipase A, a phospholipase C, a phospholipase D, a plasmin, a serine phosphatase, a tartrate resistant phosphatase, a tartrate resistant phosphatase, a threonine phosphatase, a thymidine deaminase, a tripeptidyl peptidase, a trypsin, a tyrosine phosphatase, a urokinase, a v-thrompsin, and a γ-GT.

Claim 39. (**Original**) The method of claim 38, wherein said enzyme is a caspase.

Claim 40. (**Original**) The method of claim 39, wherein said caspase is caspase 1, caspase 3, caspase 6, caspase 8, or caspase 9.

Claim 41. (**Original**) The method of claim 13, wherein multiple enzymes are simultaneously assayed.

Claim 42. (**Original**) The method of claim 13, wherein multiple enzymes are sequentially assayed.

Claim 43. (**Original**) The method of claim 13, wherein said step (b) includes measuring an intensity of said second state against time.

Claim 44. (**Original**) The method of claim 13, wherein said step (b) includes measuring a magnitude of said second state at a point of time.

Claim 45. (**Original**) The method of claim 13, wherein said substrate or analyte compound comprises more than one leaving group, and wherein each of said substrate's leaving groups is cleaved sequentially by said enzyme.

Claim 46. (**Original**) The method of claim 13, wherein said indicator group is selected from the group consisting of rhodamine 110, rhodol, fluorescein, coumarin, and derivatives thereof.

Claim 47. (**Original**) The method of claim 46, wherein said derivatives of rhodamine 110, rhodol, fluorescein and coumarin are selected from the group consisting of 4'(5')thiofluorescein, 4'(5')-aminofluorescein, 4'(5')-carboxyfluorescein, 4'(5')-chlorofluorescein, 4'(5')-methylfluorescein, 4'(5')-sulfofluorescein, 4'(5')-aminorhodol, 4'(5')-carboxyrhodol, 4'(5')-chlororhodol, 4'(5')-methylrhodol, 4'(5')-sulforhodol; 4'(5')-aminorhodamine 110, 4'(5')-sulforhodamine 110, 4'(5')thiorhodamine 110, 7-aminocoumarin, and sulfonated coumarin.

Claim 48. (**Original**) The method of claim 13, wherein said assay detects the presence or absence of an abnormality in the activity of said enzyme by comparing the production of said second state of said indicator group by said test cell

to the production of said second state of said indicator group by a reference normal cell.

Claim 49. (**Original**) The method of claim 48, wherein said abnormality is a morphological or disease state.

Claim 50. (**Original**) The method of claim 49, wherein said morphological state is an apoptotic state.

Claim 51. (**Original**) The method of claim 49, wherein said disease state is a tumorigenic state.

Claim 52. (**Original**) The method of claim 13, wherein said substrate or analyte compound contains a blocking group.

Claim 53. (**Original**) The method of claim 52, wherein said blocking group is a Cbz blocking group.

Claim 54. (**Original**) The method of claim 13, wherein said substrate or analyte compound of said enzyme and said agent that enhances said uptake are mixed during said incubation.

Claim 55. (**Original**) The method of claim 13, wherein said substrate or analyte compound of said enzyme and said agent that enhances said uptake are not mixed during said incubation.

Claims 56-95 (**Withdrawn**)